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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/439,040	11/12/99	VAN DONGEN	J 4222US

EXAMINER	
WILDER, C	
ART UNIT	**PAPER NUMBER**
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DATE MAILED: 09/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/439,040	Van Dongen et al.
Examiner	**Art Unit**
CB Wilder	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 9, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12 and 14-21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12 and 14-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The request filed on for a Continued Examination (RCE) under 37 CFR 1.114 based on Application No. 09/439,040 is acceptable and an RCE has been established. An action on the RCE follows.

Claim Rejections - 35 USC § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-12, 14, 15, and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Tkachuk et al. (Tkachuk, herein) (Science October 1990). Regarding claim 1, Tkachuk discloses a pair of nucleic acid probes having comparable size, said size being from about 10-30 kb in size, and flanking a potential breakpoint in a chromosome, each said probe being labeled with at least one different reporter molecule (page 560, "Figure 1" and col. 1, lines 5-7, 13-15 and 22-27).

Regarding claims 2 and 3, Tkachuk discloses a pair of distinct nucleic acid probes comparable size, said size being from about 10-30 kb and flanking a potential breakpoint in a chromosome, which pair of distinct nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of less that 250 kb or about 25 to 225 kb (page 560, "Figure 1" and col. 3, lines 2-8). See also *In re Petering*, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)).

Regarding claims 4 and 5, Tkachuk teach wherein the pair of distinct nucleic acid probes are labeled indirectly with at least one reporter molecule and wherein the reporter molecule is a fluorochrome (page 560, col. 1, lines 22-27).

Regarding claims 7-8, and 19-21, Tkachuk teach wherein the distinct nucleic acid probes hybridize to a single corresponding nucleic acid molecule and wherein the single corresponding nucleic acid molecule is at least a fragment of a chromosome and wherein the chromosome is not aberrant (normal) and aberrant (CML) (page 561, "Figure 3").

Claim 9 is drawn to a pair of nucleic acid probes of claim 1 which hybridize *in situ*. Tkachuk discloses wherein fluorescent *in situ* hybridization was carried out using the probes as described previously (page 560, col. 1, lines 22-27).

Regarding claim 10, Tkachuk discloses wherein the pair of distinct nucleic acid probes hybridizes *in situ* under conditions to only a few linear DNA molecules per cell (page 560, "Figure 1").

Regarding claim 11, Tkachuk discloses a method of detecting a nucleic acid molecule having a chromosomal aberration said method comprising providing a pair of distinct nucleic acid probes to analyze a sample believed to contain nucleic acid (page 559, "Abstract"), said distinct nucleic acid probes having comparable size; said size being from about 10-30 kb in size, and flanking a potential breakpoint in a chromosome, each said probe pair being labeled with at least one different reporter molecule, hybridizing the nucleic acid probe to the nucleic acid; and detecting the presence of the reporter molecule (page 560, "Figure 1" and col. 1, lines 5-7, 13-15 and 22-41).

Regarding claim 12, Tkachuk discloses a method of detecting cells suspected of having a chromosomal aberration, said method comprising providing a pair of distinct nucleic acid probes to analyze nucleic acid of said cells, said distinct nucleic acid probes having comparable size, said size being selected from the group consisting of 10-30 kb in size and flanking a potential breakpoint in a chromosome, each of said pair of distinct probes being labeled with at least one different reporter molecule; hybridizing said distinct nucleic acid probes to the nucleic acid of at least one if said cells and detecting the presence of said reporter molecule (page 559, col. 3, lines 19-23 and page 560, col. 1, lines 1-3 and 31-41).

Regarding claims 14 and 15, Tkachuk discloses wherein the chromosomal aberration is associated with hematopoietic malignancy (page 559, "Abstract").

Regarding claims 17 and 18, Tkachuk discloses wherein the distinct nucleic acid probes hybridize to a single corresponding nucleic acid molecule and wherein the single chromosome molecule is at least a fragment of a chromosome (page 561, "Figure 3").

Therefore, the claimed invention of claims 1-12, 14, 15, and 17-21 are anticipated by the reference of Tkachuk.

4. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Rowley et al. (Rowley, herein) (5,487,970 January 30, 1996). Claim 16 is drawn to a diagnostic kit comprising at least the pair of nucleic acid probes of claim 1. Rowley teaches a diagnostic kit comprising a pair of nucleic acid probes having comparable size wherein the size is from about 0.3 kb to 1.5 kb, and labels for

the probes for *in situ* hybridization procedures (col. 7, lines 19-44). Therefore, the claimed invention of claim 16 is anticipated by the reference of Rowley.

5. Applicant traverses the rejection on the following grounds: Applicant argues that Tkachuk et al. provides a probe that spans/overlap the breakpoint cluster region. A second probe is provided by Tkachuk et al. separated from the first probe which spans/ overlap the breakpoint cluster region by a distance of between 15-200 base pairs. Applicant argues that these probes are in stark contrast to the presently claimed invention where the probes are provided which lie adjacent to or flank the breakpoint cluster region and don not lie within or span or overlap the breakpoint cluster region. Applicant argues that the claimed invention specifically disclose that false positive diagnosis may arise from the (a) use of probes (such as the probes of Tkachuk) that overlap the breakpoint cluster, and (b) the use of probes (such as the probes of Tkachuk) directed against different chromosomes with juxtaposition of both signals into one signal in the case of translocation. Applicant argues that in contrast, the claimed invention provides a means to avoid such false positive diagnoses by using the claimed invention (probes lying adjacent to/ flanking, but not lying within the breakpoint cluster region on one chromosome giving rise to a split signal, e.g., two split signal) after translocation. Accordingly, the claims 1-12, 14, 15, 17-21 are not anticipated by the cited reference.

Regarding claim 16, Applicant argues that the kit discloses by Rowley et al. do not provide pairs of proteins, the particular probes specified by Rowley et al. lie adjacent to one another and are smaller than 1Kb. Applicant further argues that one of the probe (MLL 0.7 Kb) lies within the breakpoint region. Applicant argues that due to their small size, such probes could not be used in

combination with MLL 1.5 Kb for FISH detection. Applicant concludes that Rowley cannot anticipate claim 16.

6. Applicant arguments have been fully considered but they are not found persuasive for the reasons that follows: First, the courts have established that "during patent examination the pending claims must be interpreted as broadly as their terms reasonable allow" *In re Zletz, 893 f. 2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).* In this case, the claims as recited are only limited to a pair of nucleic acid probes having comparable size and flanking a potential breakpoint region of a chromosome and wherein the probes are labeled with a different reporter molecule. These limitation are recited in the reference of Tkachuk et al.. According to Webster's Collegiate Dictionary, "flanking" can be defined as " to be situated on both sides of" or "to place something on each side of ". Therefore, as noted in the prior Office actions, Tkachuk teach a pair of probes flanking (placed on both sides of) a breakpoint region. Furthermore, the argument that Applicant's probes avoids false positives diagnoses is irrelevant because the features upon which Applicant relies (i.e. ones lying adjacent to but not lying within the breakpoint cluster region on one chromosome giving rise to a split signal (two separate signals after translocation) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant has not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the reference cited or

how the amendments avoid such reference. Accordingly, the prior art rejection under 35 U.S.C. 102(b) drawn to claims 1-12, 14, 15, and 17-21 as being anticipated by Tkachuk et al. is maintained.

With regards to claim 16, it is the Examiner's position that Rowley et al. meet all of the limitations of the claimed invention. As discussed in the prior Office actions, Rowley et al. teach wherein the kit comprises 1 or more than one distinct nucleic acid probes having comparable size as given by the sequence of the probes and in figures 1 and 2. Contrary to Applicant's arguments, Rowley teach wherein the probes are 0.3 Kb to 1.5 Kb which does encompass a probe 1 Kb and larger and falls within the range Applicant recites in the claims. Likewise Rowley teach that the cloned DNA probes form both sides of a breakpoint region of a chromosome and are used with FISH to detect translocation. Therefore, the argument that Rowley teach probes lying within a breakpoint region is irrelevant to the instant invention because such a limitation is not recited in the claims. With regards to Applicant's arguments that such small probes could not be used in combination with the larger probes for FISH detection purposes is also irrelevant to the instant invention because Applicant is arguing an intended use of a product (not a method step) which carries no patentable weight (see MPEP 2144.07). Applicant has not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the reference cited or how the amendments avoid such reference. Accordingly, the prior art rejection under 35 U.S.C. 102(b) drawn to claim 16 as being anticipated by Rowley et al. is maintained.

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

September 14, 2001

W. Gary Jones
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9/17/01